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09/938,677	08/24/2001	Robert H. Harris	13095	2566

7590 06/24/2004  
Scully, Scott, Murphy & Presser  
400 Garden City Plaza  
Garden City, NY 11530

EXAMINER

LUKTON, DAVID

ART UNIT PAPER NUMBER

1653

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/938,677

**Applicant(s)**

HARRIS, ROBERT H.

**Examiner**

David Lukton

**Art Unit**

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2,5-19,51,56,58-62 and 73-89 is/are pending in the application.
- 4a) Of the above claim(s) 7,11-13 and 84-89 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,6,8-10,14,16-19,51,56 and 73-78 is/are rejected.
- 7) ☒ Claim(s) 5,15,58-62 and 79-83 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

Pursuant to the directives of the amendment filed 4/9/04, claims 1, 2, 6, 7, 51 have been amended, claims 3 and 4 cancelled, and claims 75-89 added.

Claims 1, 2, 5-19, 51, 56, 58-62 and 73-89 are now pending. Claims 7, 11-13, 84-89 are withdrawn from consideration, since they do not encompass the elected specie.

Claims 1, 2, 5, 6, 8-10, 14-19, 51, 56, 58-62 and 73-83 are examined in this Office action

Applicants' arguments filed 4/9/04 have been considered and found persuasive in part. The rejection of claim 1 over Bialer (WO 99/43309) is withdrawn.

. . . . .

The following abbreviations are used hereinbelow:

“**EWG**” represents an electron-withdrawing group

“**EDG**” represents an electron-donating group

“**EWG/EDG**” signifies that a group may be either electron-donating, or electron-withdrawing



Claim 8 is rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The dependence of claim 8 on claim 6 is not proper. Claim 8 permits R<sub>3</sub> to be alkyl that is

substituted with an EWG/EDG; however, while claim 6 does permit  $R_3$  to be alkyl, claim 6 does not permit  $R_3$  to be alkyl that is substituted with an EWG/EDG.



The following is a quotation of the appropriate paragraphs of 35 U.S.C §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

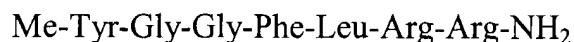
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 6, 8, 56 are rejected under 35 U.S.C. §102(b) as being anticipated by Yoshino (USP 4,707,468).

Yoshino discloses (cols 5-12) various analgesic peptides. Consider, for example, the first of these, which is the following:



This may be characterized in one of a few different ways, including the following:

First characterization:

$R_1$  = methyl substituted with EWG/EDG  
 $R_2$  = hydrogen;  
 $R_3$  = benzyl  
 $R$  = alkyl substituted with EWG/EDG;

Second characterization:

$R_1$  = methyl substituted with EWG/EDG  
 $R_2$  = hydrogen;  
 $R_3$  = alkyl  
 $R$  = methyl substituted with EWG/EDG;

Third characterization:

$R_1$  = methyl substituted with EWG/EDG  
 $R_2$  = hydrogen;  
 $R_3$  = alkyl substituted with EWG/EDG  
 $R$  = hydrogen

In the response filed 4/9/04, applicants have argued that the compounds of the instant claims are limited to just two amide groups, whereas the Yoshino compounds require six amide groups. However, applicants premise regarding the instant claims is not correct. The instant claims permit  $R$  to be an alkyl group that is substituted with an EWG/EDG. As applicants appear to recognize (page 20, line 7+, specification), any substituent which is

electronically different from hydrogen is encompassed. There are no other limitations. Virtually all substituents are electronically different from hydrogen, as such, all substituents other than hydrogen would be encompassed by the term "EWG" or "EDG". The fact that a given substituent may contain an amide bond (or a few amide bonds) does not, by any analysis, make that substituent equivalent to hydrogen. Accordingly, peptides of any length would be encompassed.



Claims 1, 2, 8, 16-19, 51, 56, 73 are rejected under 35 U.S.C. §102(b) as being anticipated by Gesellchen (USP 4,510,082).

Gesellchen discloses (col 9, line 45+) compounds for treatment of pain. Among them is the compound recited in claim 17 (col 18, line 35+). This compound falls within the instant claims when the substituent variables correspond as follows:

R = methyl substituted with carboxyl

R1 = aryl loweralkyl substituted with EWG/EDG

R2 = hydrogen

R3 = methyl substituted with methoxy

Thus, the claims are anticipated.



Claims 1, 2, 8, 16-19, 73, 75 are rejected under 35 U.S.C. §102(a) as being anticipated by Seko (EP 0,997,147).

Seko discloses various compounds for treating pain. Among them are the compounds disclosed on pages 24-27. For example, the following would be encompassed (applicants' substituent variables):

R = benzyl substituted with EWG/EDG

R1 = alkyl substituted with EWG/EDG

R2 = hydrogen

R3 = methyl substituted with cyclopentylmethoxy

Thus, the claims are anticipated.



The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1, 2, 8, 16-19, 73 are rejected under 35 U.S.C. §103 as being unpatentable over Montana (USP 6,180,611).

Montana discloses various compounds which can be used to treat any of several inflammatory conditions. Among those conditions (col 54, line 33) is migraine headaches.

Among the compounds disclosed is that of example 71; this compound contains O-methylserine and may be found at col 49, line 11+.

R = alkyl substituted with EWG/EDG

R1 = alkyl substituted with EWG/EDG

R2 = hydrogen

R3 = methyl substituted with methoxy

The pharmacologist of ordinary skill would reason that if a migraine headache can be successfully treated, the pain associated therewith would be mitigated.

Thus, the claims are anticipated.



Claims 1, 2, 8, 16-19, 73 are rejected under 35 U.S.C. §103 as being unpatentable over Montana (USP 6,180,611) in view of Konttinen Y. T. (*Arthritis and rheumatism* 37 (7) 965-82, 1994)



One of the compounds disclosed by Montana is indicated above. Also disclosed (e.g., col 54, line 41) is treatment of arthritis. Montana does not disclose that there is pain associated with arthritis. Kontinen discloses that pain accompanies arthritis. Accordingly, the pharmacologist of ordinary skill would reason that if arthritis can be successfully treated, the pain associated therewith will be mitigated.

Thus, the claims are rendered obvious.



Claims 1, 2, 16-19, 73, 77, 78 are rejected under 35 U.S.C. §103 as being unpatentable over Laruelle (USP 4518587).

Laruelle discloses various dipeptides containing hydroxytryptophan. Among them is (col 7, line 45+) N-acetyl-(OH)Trp-Tyr-OMe.

Laruelle discloses (col 17, line 31+) that all of the compounds are effective analgesics. This compound falls within the scope of instant claim 1 when the substituent variables are as follows:

R = alkyl substituted with EWG/EDG

R1 = methyl

R2 = hydrogen

R3 = loweralkyl heterocyclic



Claims 1, 2, 6, 8, 16-19, 73, 74, 78 are rejected under 35 U.S.C. §103 as being unpatentable over Balasubramanium (USP 6,737,408).

Balasubramanium discloses various peptides which can be used (col 9, line 56) for treatment of pain. Among them is the following (col 18, line 12):



This peptide falls within the scope of claim 1 according to either of the following characterizations:

First characterization:

R = alkyl substituted with EWG/EDG

R1 = methyl

R2 = hydrogen

R3 = aryl loweralkyl

Second characterization:

R = hydrogen

R1 = alkyl substituted with EWG/EDG

R2 = hydrogen

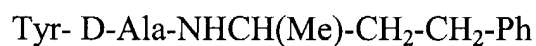
R3 = loweralkyl heterocyclic

Thus, the claims are rendered obvious.



Claims 1, 2, 6, 8-10, 14, 16-19, 51, 56, 73-75 are rejected under 35 U.S.C. §103 as being unpatentable over Morgan (USP 4,533,657).

Morgan discloses various compounds for inducing analgesia. Among them is (col 9, line 50+) the following



This corresponds to the substituent variables (of claim 1) as follows:

R = aryl lower alkyl

R1 = alkyl substituted with EWG/EDG

R2 = hydrogen

R3 = methyl

Thus, the claims are rendered obvious.



Claims 1, 2, 6, 16-19, 73, 74 are rejected under 35 U.S.C. §103 as being unpatentable over Fink (USP 5508266).

Fink discloses (col 1) compounds of formula I which can be used for treating pain. Various

species are disclosed at col 14, line 45+. This corresponds to the substituent variables (of claim 1) as follows:

R = alkyl substituted with EWG/EDG

R1 = arylalkyl substituted with EWG/EDG

R2 = methyl

R3 = methyl

Thus, the claims are rendered obvious.



Claims 1, 2, 16-19, 75, 76 are rejected under 35 U.S.C. §103 as being unpatentable over Schwender (USP 6037324).

Schwender discloses (col 12, line 20+) that the disclosed compounds can be used to treat IBD (inflammatory bowel disease). Also disclosed (col 2, line 39) is that patients suffering from IBD experience pain as a result of the disorder. Among the compounds disclosed are the following (col 7, line 40+):

Idc-Asp-Thr-NH-benzyl

Bpc-Asp-Thr-NH-benzyl

These compounds can be characterized in either of two ways:

First characterization:

R = benzyl

R1 = alkyl substituted with EWG/EDG

R2 = hydrogen

R3 = ethyl substituted with hydroxyl

Second characterization:

R = alkyl substituted with EWG/EDG

R1 = heterocycle

R2 = hydrogen

R3 = alkyl substituted with carboxyl

Thus, the skilled artisan would reason that if IBD can be successfully treated, the pain associated therewith will be alleviated.



Claims 1, 2, 16-19, 73 are rejected under 35 U.S.C. §103 as being unpatentable over Eisenbach-Schwartz (USP 6,126,939).

Eisenbach-Schwartz discloses various di- and tripeptides, and further discloses (col 4, line 56) that the peptides are effective analgesics. All of the tripeptides disclosed in col 3, lines 48-61 are encompassed by claim 1.

Thus, the claims are rendered obvious.



Claims 1, 2, 6, 8, 16, 18, 73, 56 are rejected under 35 U.S.C. §103 as being unpatentable over Yoshino (USP 4,707,468) in view of Lowry, Thomas (*Mechanism and Theory in Organic Chemistry*, pages 60-70, Harper & Row, New York, 1976).

The teachings of Yoshino are disclosed above. Yoshino does not disclose that groups containing amide bonds will be electronically different from hydrogen. Lowry discusses linear free energy relationships, specifically the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been evident to the physical organic chemist of ordinary skill that substituents such as the following would not be electronically identical to hydrogen, when occupying the *meta*- or *para*- position of benzoic acid:



The claims do not even require that the physical organic chemist of ordinary skill make a determination as to whether the substituent in question is going to be more electronegative than hydrogen, or more electropositive; the claims require only that the chemist recognize that there

would be some difference between the electron-donating propensity of the substituent in question, and that of hydrogen. Certainly, if benzoic acid were substituted in the *para*-position with an amino acid or peptide, there would be a discernable effect on the acidity (relative to benzoic acid itself).

Thus, the claims are rendered obvious.



Claims 1, 2, 8, 16-19, 51, 56, 73 are rejected under 35 U.S.C. §103 as being unpatentable over Gesellchen (USP 4,510,082) in view of Lowry, Thomas (*Mechanism and Theory in Organic Chemistry*, pages 60-70, Harper & Row, New York, 1976).

The teachings of Gesellchen are indicated above. Gesellchen does not disclose that groups containing amide bonds will be electronically different from hydrogen.

Lowry discusses linear free energy relationships, specifically, the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been evident to the physical organic chemist of ordinary skill that substituents such as the following would not be electronically identical to hydrogen, when occupying the *meta*- or *para*- position of benzoic acid:



The claims do not even require that the physical organic chemist of ordinary skill make a determination as to whether the substituent in question is going to be more electronegative than hydrogen, or more electropositive; the claims require only that the chemist recognize that there would be some difference between the electron-donating propensity of the substituent in question, and that of hydrogen. Certainly, if benzoic acid were substituted in the *para*-position with an amino acid or peptide, there would be a discernable effect on the acidity (relative to benzoic acid itself).

Thus, the claims are rendered obvious.



Claims 1, 2, 8, 16-19, 73, 75 are rejected under 35 U.S.C. §103 as being unpatentable over Seko (EP 0,997,147) in view of Lowry, Thomas (*Mechanism and Theory in Organic Chemistry*, pages 60-70, Harper & Row, New York, 1976).

The teachings of Seko are indicated above. Seko does not disclose that substituent groups that contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Lowry discusses linear free energy relationships, specifically, the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been



evident to the physical organic chemist of ordinary skill that substituents which contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Thus, the claims are rendered obvious.



Claims 1, 2, 8, 16-19, 73 are rejected under 35 U.S.C. §103 as being unpatentable over Montana (USP 6,180,611) in view of Lowry, Thomas (*Mechanism and Theory in Organic Chemistry*, pages 60-70, Harper & Row, New York, 1976).

The teachings of Montana are indicated above. Montana does not disclose that substituent groups that contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Lowry discusses linear free energy relationships, specifically, the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been evident to the physical organic chemist of ordinary skill that substituents which contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Thus, the claims are rendered obvious.



Claims 1, 2, 8, 16-19, 73 are rejected under 35 U.S.C. §103 as being unpatentable over Montana (USP 6,180,611) in view of Konttinen Y. T. (*Arthritis and rheumatism* 37 (7)

965-82, 1994) further in view of

The teachings of Montana and Konttinen are indicated above. Neither of Montana and Konttinen discloses that substituent groups that contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Lowry discusses linear free energy relationships, specifically, the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been evident to the physical organic chemist of ordinary skill that substituents which contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Thus, the claims are rendered obvious.



Claims 1, 2, 16-19, 73, 77, 78 are rejected under 35 U.S.C. §103 as being unpatentable over Laruelle (USP 4518587) in view of Lowry, Thomas (*Mechanism and Theory in Organic Chemistry*, pages 60-70, Harper & Row, New York, 1976).

The teachings of Laruelle are indicated above. Laruelle does not disclose that substituent groups that contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Lowry discusses linear free energy relationships, specifically, the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and

electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been evident to the physical organic chemist of ordinary skill that substituents which contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Thus, the claims are rendered obvious.



Claims 1, 2, 6, 8, 16-19, 73, 74, 78 are rejected under 35 U.S.C. §103 as being unpatentable over Balasubramanium (USP 6,737,408) in view of Lowry, Thomas (*Mechanism and Theory in Organic Chemistry*, pages 60-70, Harper & Row, New York, 1976).

The teachings of Balasubramanium are indicated above. Balasubramanium does not disclose that substituent groups that contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Lowry discusses linear free energy relationships, specifically, the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been evident to the physical organic chemist of ordinary skill that substituents which contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Thus, the claims are rendered obvious.



Claims 1, 2, 6, 8-10, 14, 16-19, 51, 56, 73-75 are rejected under 35 U.S.C. §103 as being unpatentable over Morgan (USP 4,533,657) in view of Lowry, Thomas (*Mechanism and Theory in Organic Chemistry*, pages 60-70, Harper & Row, New York, 1976).

The teachings of Morgan are indicated above. Morgan does not disclose that substituent groups that contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Lowry discusses linear free energy relationships, specifically, the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been evident to the physical organic chemist of ordinary skill that substituents which contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Thus, the claims are rendered obvious.



Claims 1, 2, 6, 16-19, 73, 74 are rejected under 35 U.S.C. §103 as being unpatentable over Fink (USP 5508266) in view of Lowry, Thomas (*Mechanism and Theory in Organic Chemistry*, pages 60-70, Harper & Row, New York, 1976).

The teachings of Fink are indicated above. Fink does not disclose that substituent groups that contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Lowry discusses linear free energy relationships, specifically, the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been evident to the physical organic chemist of ordinary skill that substituents which contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Thus, the claims are rendered obvious.



Claims 1, 2, 16-19, 75, 76 are rejected under 35 U.S.C. §103 as being unpatentable over Schwender (USP 6,037,324) in view of Lowry, Thomas (*Mechanism and Theory in Organic Chemistry*, pages 60-70, Harper & Row, New York, 1976).

The teachings of Schwender are indicated above. Schwender does not disclose that substituent groups that contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Lowry discusses linear free energy relationships, specifically, the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been evident to the physical organic chemist of ordinary skill that substituents which contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Thus, the claims are rendered obvious.



Claims 1, 2, 16-19, 73 are rejected under 35 U.S.C. §103 as being unpatentable over Eisenbach-Schwartz (USP 6,126,939) in view of Lowry, Thomas (*Mechanism and Theory in Organic Chemistry*, pages 60-70, Harper & Row, New York, 1976).

The teachings of Eisenbach-Schwartz are indicated above. Eisenbach-Schwartz does not disclose that substituent groups that contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Lowry discusses linear free energy relationships, specifically, the effects of various substituents on the ionization of benzoic acid. Specific examples of electron-donating and electron-withdrawing substituents are provided in table 2.1 (page 62). It would have been evident to the physical organic chemist of ordinary skill that substituents which contain nitrogen and/or carbon atoms will be electronically different from hydrogen.

Thus, the claims are rendered obvious.



No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

*De Luca*

DAVID LUKTON  
PATENT EXAMINER  
GROUP 1000